Amendments to the Specification

Please replace the section beginning at page 1, line 3, with the following redlined section.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application No. 09/151,409, filed September 10, 1998, issued as U.S. Patent 6,716,433 on April 6, 2004, which application claims the benefit of United States Provisional Application No. 60/058,635, filed September 12, 1997, which applications are incorporated by reference in their entirety.

Please replace the paragraph beginning at page 9, line 3, with the following redlined paragraph.

Expression vectors transfected into prokaryotic host cells generally comprise one or more phenotypic selectable markers such as, for example, a gene encoding proteins that confer antibiotic resistance or that supplies an auxotrophic requirement, and an origin of replication recognized by the host to ensure amplification within the host. Other useful expression vectors for prokaryotic host cells include a selectable marker of bacterial origin derived from commercially available plasmids. This selectable marker can comprise genetic elements of the cloning vector pBR322 (ATCC 37017). Briefly, pBR322 contains genes for ampicillin and tetracycline resistance and thus provides simple means for identifying transformed cells. The pBR322 "backbone" sections are combined with an appropriate promoter and a mammalian ETF structural gene sequence. Other commercially available vectors include, for example, pKK223-3 (Pharmacia® Fine Chemicals, Uppsala, Sweden), pQE30 (6xHis-tag expression vector), and pGEM1 (Promega® Biotec, Madison, WI, USA).

Please replace the paragraph beginning at page 16, line 23, with the following redlined paragraph.

Transformed *E. coli* were grown in a shaking incubator to log phase in 1l of LB containing 100 μg/ml ampicillin and 25 μg/ml kanamycin. IPTG (2 mM) was added for the final

four hours of growth. The cell pellet was suspended in 30 ml PBS and lysed in a French pressure cell at 1000 psi. The hexavalent protein was purified from the supernatant using Ni-NTA resin according to the protocol provided by the manufacturer (Qiagen®, Valencia, CA). The elution buffer containing the protein was concentrated from 15 ml to 5 ml in a spin filter (ULTRAFREE®-15, Millipore®). Final purification was accomplished by gel filtration over SUPERDEX™ 75 (prep grade, Pharmacia® Biotech). The active fraction was identified by Western blots (Dale, J.B. and Beachey, E.H., "Multiple heart-cross-reactive epitopes of streptococcal M proteins," *J. Exp. Med. 161*:113-122, 1985) using rabbit antiserum against pep M24 (Beachey et al., "Purification and properties of M protein extracted from group A streptococci with pepsin: Covalent structure of the amino terminal region of the type 24 M antigen," *J. Exp. Med. 145*:1469-1483, 1977). Total protein concentration was determined by standard methods and the sample was diluted in PBS to contain 200 μg/ml of hexavalent protein. Purity of the samples was determined by gel scanning (PHOTOSHOP™ digital image and COLLAGE™ image analysis).

Please replace the paragraph beginning at page 20, line 14, with the following redlined paragraph.

Direct mouse protection tests are similarly performed except that mice are actively immunized with M protein vaccine prior to the challenge infections. Each mouse receives 25-50 ~~ug~~ μg vaccine in alum given intramuscularly (i.m.) at time 0, 4 weeks, and 8 weeks. Challenge infections are performed ten weeks after the first injection. Control animals are sham immunized with alum alone. The LD50 is calculated and significance is determined using Fisher's exact test.

Please replace the paragraph beginning at page 21, line 23, with the following redlined paragraph.

To assure that none of the M protein vaccines evokes tissue-crossreactive antibodies, indirect immunofluorescence assays are performed using frozen sections of human heart, kidney, and brain (Dale, J.B. and Beachey E.H., "Protective antigenic determinant of

streptococcal M protein shared with sarcolemmal membrane protein of human heart," *J. Exp. Med. 156*:1165-1176, 1982). Thin sections of tissue obtained at autopsy (4~~um~~ um) are prepared on microscope slides and stored in a sealed box at -70°C until use. Test serum is diluted 1:5 in PBS and dropped onto the tissue section. Control slides are made with preimmune serum and PBS. The slides are incubated at ambient temperature for 30 minutes and then washed three times in PBS in a slide holder. Fluorescein-labeled goat anti-IgG/IgM/IgA is diluted 1:40 in PBS and dropped onto the slides which are again washed, dried, and mounted with 1% ~~Gelvatol~~ gelvatol (polyvinyl alcohol) and a coverslip. Fluorescence is detected using a Zeiss® Axiophot® microscope equipped with a xenon light source. Immunofluorescence is recorded using a scale of 0-4+, with 0 being no fluorescence and 4+ being that obtained with a standard, positive antiserum raised in rabbits against whole type 5 M protein (Dale, J.B. and Beachey, E.H., "Multiple heart-cross-reactive epitopes of streptococcal M proteins," *J. Exp. Med. 161*:113-122, 1985).